K130053

BioPlex® 2200 Celiac IgA and IgG 510(k) Summary

Bio-Rad Laboratories hereby submits this 510(k) in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. This summary of 510(k) safety and effectiveness information provides detail as a basis for a determination of substantial equivalence for the BioPlex® 2200 Celiac IgA and IgG kits.

510(k) Number:
K130053

Summary Preparation Date:
August 14, 2013

Applicant:
Bio-Rad Laboratories

SEP 19 2013

Contact:
Juang Wang
Regulatory Affairs Representative

Purpose for Submission:
New Device

Measurand:
IgA and IgG antibodies to tissue Transglutaminase (tTG)
IgA and IgG antibodies to deamidated gliadin peptide (DGP)

Type of Test:
Semi-Quantitative multiplexed flow, bead-based immunoassay

Proprietary and Established Names:
BioPlex® 2200 Celiac IgA kit
BioPlex® 2200 Celiac IgG kit
BioPlex® 2200 Celiac IgA Calibrator Set
BioPlex® 2200 Celiac IgA Control Set
BioPlex® 2200 Celiac IgG Calibrator Set
BioPlex® 2200 Celiac IgG Control Set

Regulatory Information:

Product Code	Classification	Regulation Section	Panel
Autoantibodies, endomysial(tissue transglutaminase) (MVM)	Class II	21 CFR § 866.5660, Multiple autoantibodies immunological test system.	Immunology (82)
Antibodies, Gliadin (MST)	Class II	21 CFR § 866.5750, Radioallergosorbent (RAST) immunological test system.	Immunology (82)
Calibrator, Multi-Analyte Mixture (JIX)	Class II	21 CFR § 862.1150 – Calibrator	Clinical Chemistry (75)
Multi-Analyte Controls All kinds(assayed) (JJY)	Class I	21 CFR § 862.1660 – Quality Control Material (Assayed and Unassayed)	Clinical Chemistry (75)

Intended Use:

1. Intended use(s):

   BioPlex® 2200 Celiac IgA Kit

   The BioPlex 2200 Celiac IgA kit is an *in vitro* multiplex flow immunoassay intended for the semi-quantitative detection of IgA autoantibodies to deamidated gliadin peptide (DGP) and tissue Transglutaminase (tTG) in human serum. In conjunction with clinical findings and other diagnostic tests, the test system is used as an aid in the diagnosis of Celiac Disease (gluten-sensitive enteropathy).

   The BioPlex 2200 Celiac IgA kit is intended for use with the Bio-Rad BioPlex 2200 System.

   BioPlex® 2200 Celiac IgG Kit

   The BioPlex 2200 Celiac IgG kit is an *in vitro* multiplex flow immunoassay intended for the semi-quantitative detection of IgG autoantibodies to deamidated gliadin peptide (DGP) and tissue Transglutaminase (tTG) in human serum. In conjunction with clinical findings and other diagnostic tests, the test system is used as an aid in the diagnosis of Celiac Disease (gluten-sensitive enteropathy).

   The BioPlex 2200 Celiac IgG kit is intended for use with the Bio-Rad BioPlex 2200 System.

BioPlex® 2200 Celiac IgA Calibrator Set

The BioPlex 2200 Celiac IgA Calibrator Set is intended for the calibration of the BioPlex 2200 Celiac IgA Reagent Pack.

BioPlex® 2200 Celiac IgG Calibrator Set

The BioPlex 2200 Celiac IgG Calibrator Set is intended for the calibration of the BioPlex 2200 Celiac IgG Reagent Pack.

BioPlex® 2200 Celiac IgA Control Set

The BioPlex 2200 Celiac IgA Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 Celiac IgA Reagent Pack in the clinical laboratory. The performance of the BioPlex Celiac IgA Control Set has not been established with any other anti-tissue Transglutaminase (tTG) and anti-Deamidated Gliadin Peptide IgA assays.

BioPlex® 2200 Celiac IgG Control Set

The BioPlex 2200 Celiac IgG Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and BioPlex 2200 Celiac IgG Reagent Pack in the clinical laboratory. The performance of the BioPlex Celiac IgG Control Set has not been established with any other anti-tissue Transglutaminase (tTG) and anti-Deamidated Gliadin Peptide IgG assays.

2. Indication(s) for use:
   Same as Intended Use

3. Special conditions for use statement(s):
   For prescription use only

4. Special instrument requirements:
   Bio-Rad BioPlex® 2200 System

Device Description:

BioPlex® 2200 Celiac IgA and IgG kits include the following components:

- One (1) 10 mL vial of Bead Set, containing dyed beads coated with recombinant antigens; an Internal Standard bead (ISB), a Serum Verification bead (SVB) and IgA Verification Bead (AVB) (in Celiac IgA only), in MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with Glycerol and protein stabilizer (bovine and porcine). ProClin 300 ($\leq 0.3\%$), sodium benzoate ($\leq 0.1\%$) and sodium azide ($< 0.1\%$) are added as preservatives.

- One (1) 5 mL vial of Conjugate, containing phycoerythrin conjugated murine monoclonal anti-human IgA or IgG and phycoerythrin conjugated sheep anti-human FXIII in MOPS (3-[N-Morpholino] propanesulfonic acid) buffer supplemented with bovine protein stabilizers. ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) are added as preservatives.
- One (1) 10 mL vial of Sample Diluent, containing bovine and murine protein stabilizers in triethanolamine buffer. ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) are added as preservatives.

BioPlex 2200 Celiac IgA and IgG Calibrator Sets contain nine (9) 0.5 mL vials of human antibodies to tTG and DGP in a buffer supplemented with protein stabilizer (porcine for IgA and porcine/human for IgG) with ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.

BioPlex 2200 Celiac IgA and IgG Control Sets contain four (4) 1.5 mL vials of Positive Controls of human antibodies to tTG or DGP and two vials of Negative Controls in a human serum matrix made from defibrinated plasma; and, in a human serum matrix made from defibrinated plasma with ProClin 300 (≤ 0.3%), sodium benzoate (≤ 0.1%) and sodium azide (< 0.1%) as preservatives.

Additional materials required but not supplied include BioPlex 2200 Sheath Fluid containing Phosphate Buffered Saline (PBS) with ProClin 300 (≤0.03%), and sodium azide (<0.1%) as preservatives; and BioPlex 2200 Wash Solution containing Phosphate Buffered Saline (PBS) and Tween 20 with ProClin 300 (≤0.03%) and sodium azide (<0.1%) as preservatives.

Substantial Equivalence Information:

1. Predicate device name(s):
   INOVA QUANTA Lite h-tTG IgA
   INOVA QUANTA Lite h-tTG IgG
   INOVA QUANTA Lite Gliadin IgA II
   INOVA QUANTA Lite Gliadin IgG II

2. Predicate 510(k) number(s):
   K011566, K011570, K052143, K052142

3. Comparison with predicate:

Similarities			
Item	Device: BioPlex 2200 Celiac IgA and IgG Kits	Predicate: INOVA QUANTA Lite h-tTG IgA and IgG Kits	Predicate: INOVA QUANTA Lite Gliadin IgA II and IgG II Kits
Intended Use	Semi-quantitative detection of IgA and IgG autoantibodies to deamidated gliadin peptide (DGP) and tissue Transglutaminase (tTG) in human serum. In conjunction with clinical findings and other diagnostic tests, the test system is used as an aid in the diagnosis of Celiac Disease (gluten-sensitive enteropathy).	Semi-quantitative detection of IgA and IgG autoantibodies to tissue Transglutaminase (endomysium) in human serum. Detection of these antibodies is an aid in diagnosis of certain gluten sensitive enteropathies such as celiac disease and dermatitis herpetiformis.	Semi-quantitative detection of gliadin IgA and IgG antibodies in human serum. The presence of gliadin antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of celiac disease.
Sample Type	Serum	Serum	Serum
Assay Type	Semi-quantitative	Same	Same
Analyte Detected	Human IgA or IgG antibodies to human tissue transglutaminase	Same	Not Applicable
	Human IgA or IgG antibodies to deamidated gliadin peptide	Not Applicable	Same

Differences			
Item	Device: BioPlex 2200 Celiac IgA and IgG Kits	Predicate: INOVA QUANTA Lite h-tTG IgA and IgG Kits	Predicate: INOVA QUANTA Lite Gliadin IgA II and IgG II Kits
Assay Technology	Automated multiplex flow immunoassay	Manual, microtiter plate format, Enzyme-linked Immunosorbent assay (ELISA)	Manual, microtiter plate format, Enzyme-linked Immunosorbent assay (ELISA)
Capture Antigen	Recombinant tTG protein and DGP antigen	Native human tissue transglutaminase (h-tTG)	Synthetic, deamidated peptide
Conjugate	Phycoerythrin conjugated	Goat anti-human IgG	Goat anti-human IgG

Differences			
Item	Device: BioPlex 2200 Celiac IgA and IgG Kits	Predicate: INOVA QUANTA Lite h-tTG IgA and IgG Kits	Predicate: INOVA QUANTA Lite Gliadin IgA II and IgG II Kits
Antibody	murine monoclonal anti-human IgA or IgG	or IgA HRP-conjugated antibody solution	or IgA HRP-conjugated antibody solution
Substrate	None	Tetramethylbenzidine (TMB) Chromogen	Tetramethylbenzidine (TMB) Chromogen
Signal Detection	Fluorescence	Color, read at 450nm	Color, read at 450nm
Solid Phase	Antigen-coated paramagnetic microbead reagent	Antigen-coated solid phase microtiter wells	Antigen-coated solid phase microtiter wells
Calibrator(s)	5 levels of Calibrator for both IgA and IgG	1 level of Low Positive control	1 level of Low Positive control
Control	One Negative and one Positive Control	One Negative, one low Positive, and one high Positive Controls	One Negative, one low Positive, and one high Positive Controls
Assay range	Anti-tTG: IgA: 0.5 to 250 U/mL IgG: 0.8 to 250 U/mL Anti-DGP: IgA: 0.2 to 250 U/mL IgG: 0.4 to 250 U/mL	Not Applicable	Not Applicable
Calibrators and Controls	Sold Separately	Kit components	Kit components
Quantitation	Results are determined from a standard calibration curve utilizing a 4-PL (4-Parameter Logistic) curve fitting.	One point calculation from the OD of the low positive control.	One point calculation from the OD of the low positive control.
Instrumentation	Bio-Rad BioPlex 2200 system	Spectrophotometer	Spectrophotometer

Standard/Guidance Document Referenced (if applicable):
CEN 13640:2002, Stability Testing of In Vitro Diagnostic Reagents
EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition.
EP06-A, Evaluation of Linearity of Quantitative Measurement, Approved Guideline, Second Edition.
EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition

EP09-A2IR, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, Second Edition (Interim Revision).
EP12-A2, User Protocol for Evaluation of Qualitative test Performance, Approved Guideline, Second Edition.
EP14-A2, Evaluation of Matrix Effects, Approved Guideline, Second Edition
EP15-A2, User Verification of Performance for Precision and Trueness, Approved Guideline, Second Edition.
EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantification, Approved Guideline.

Test Principle:
The BioPlex 2200 Celiac IgA and IgG kits use a multiplexed micro particle bead-based immunoassay for the semi-quantitative detection of IgA and IgG antibodies to tissue Transglutaminase and deamidated gliadin peptide in human serum using the Luminex flow cytometry technology.

In the BioPlex Celiac IgA and IgG assays, two (2) different populations of dyed beads are coated with antigens associated with celiac disease (recombinant antigens). The BioPlex 2200 System combines an aliquot of patient sample, sample diluent, and bead set reagent into a reaction vessel. The mixture is incubated at 37°C. After a wash cycle, anti-human IgA or IgG antibody conjugated to phycoerythrin (PE) is added to the dyed beads and this mixture is incubated at 37°C. The excess conjugate is removed in another wash cycle, and the beads are re-suspended in wash buffer. The bead mixture then passes through the detector. The identity of the dyed beads is determined by the fluorescence of the dyes, and the amount of antibody captured by the antigen is determined by the fluorescence of the attached PE. Raw data is calculated in relative fluorescence intensity (RFI).

Two additional dyed beads, Internal Standard Bead (ISB) and Serum Verification Bead (SVB) are present in each reaction mixture to verify detector response and the addition of serum to the reaction vessel. An additional control bead, IgA Verification Bead (AVB) has been included for the Celiac IgA kit to flag results for samples with deficient IgA levels. Refer to the BioPlex 2200 System Operation Manual for more information on internal quality control beads.

The system is calibrated using a set of nine (9) distinct calibrator vials, supplied separately by Bio-Rad Laboratories. For anti-tTG, five (5) vials, representing five (5) different antibody concentrations, are used for semi-quantitative calibration for anti-tTG IgA and IgG. For anti-DGP, five (5) vials, representing five (5) different antibody concentrations, are used for semi-quantitative calibration for anti-DGP IgA and IgG. The result for each of these antibodies is expressed in Units/mL (U/mL).

Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

Precision testing of the BioPlex® 2200 Celiac IgA and IgG kits on the BioPlex® 2200 instrument was performed in accordance with CLSI EP5-A2. A serum panel consisting of samples spanning the measuring range was assayed in replicate twice daily over 20 days (n=80). One positive and one negative control were included. The data were analyzed for within-run, between-run, between-day, and total precision and the mean U/mL, standard deviation and percent coefficient of variation are summarized below:

BioPlex® 2200 Celiac IgA – Anti-tTG

Sample Type	N	Mean U/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Negative	80	6.3	0.4	6.2%	0.2	3.3%	0.4	6.3%	0.6	9.4%
High Negative	80	6.2	0.4	6.1%	0.0	0.0%	0.4	5.8%	0.5	8.4%
Near Cutoff	80	12.5	0.9	6.9%	0.0	0.0%	1.1	8.4%	1.4	10.9%
Near Cutoff	80	15.7	0.8	5.2%	0.7	4.4%	0.8	5.0%	1.3	8.5%
Low Positive	80	36.5	2.3	6.4%	1.2	3.4%	2.6	7.1%	3.7	10.2%
Low Positive	80	38.4	2.2	5.8%	0.0	0.0%	3.0	7.8%	3.7	9.7%
Mid Positive	80	108.4	6.3	5.8%	3.4	3.1%	7.9	7.3%	10.7	9.9%
Mid Positive	80	94.8	6.5	6.8%	0.0	0.0%	5.3	5.6%	8.4	8.9%
High Positive	80	210.9	10.9	5.2%	0.0	0.0%	11.8	5.6%	16.1	7.6%
High Positive	80	227.7	8.2	3.6%	5.5	2.4%	9.0	3.9%	13.3	5.8%
Negative Control	80	1.3	0.1	5.6%	0.0	0.0%	0.1	5.1%	0.1	7.5%
Positive Control	80	65.7	2.4	3.7%	1.1	1.7%	1.6	2.5%	3.1	4.7%

BioPlex® 2200 Celiac IgA – Anti-DGP

Sample Type	N	Mean U/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Negative	80	8.3	0.5	6.4%	0.0	0.0%	0.7	8.9%	0.9	11.0%
High Negative	80	4.1	0.3	6.7%	0.3	6.5%	0.2	4.6%	0.4	10.4%
Near Cutoff	80	16.1	0.7	4.6%	0.3	2.0%	0.7	4.2%	1.1	6.5%
Near Cutoff	80	15.3	0.9	6.0%	0.0	0.0%	0.5	3.3%	1.1	6.8%
Low Positive	80	34.5	1.8	5.1%	0.0	0.0%	1.0	2.9%	2.0	5.9%
Low Positive	80	33.9	2.0	5.8%	0.7	1.9%	2.1	6.3%	3.0	8.8%
Mid Positive	80	96.8	6.1	6.3%	0.0	0.0%	2.8	2.9%	6.7	6.9%
Mid Positive	80	98.5	4.6	4.7%	0.0	0.0%	5.7	5.8%	7.3	7.5%
High Positive	80	185.5	8.4	4.5%	0.0	0.0%	12.2	6.6%	14.8	8.0%
High Positive	80	200.3	9.3	4.6%	0.0	0.0%	10.9	5.5%	14.3	7.2%
Negative Control	80	2.0	0.2	7.5%	0.0	1.7%	0.1	6.8%	0.2	10.3%
Positive Control	80	60.5	2.0	3.4%	0.8	1.3%	2.5	4.1%	3.3	5.4%

BioPlex® 2200 Celiac IgG – Anti-tTG

Sample Type	N	Mean U/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Negative	80	7.7	0.5	6.2%	0.3	3.3%	0.7	9.4%	0.9	11.7%
High Negative	80	9.3	0.5	5.6%	0.5	5.7%	1.2	13.2%	1.4	15.4%
Near Cutoff	80	14.6	0.9	5.8%	0.4	2.6%	1.2	8.4%	1.5	10.5%

Near Cutoff	80	15.7	1.3	8.1%	0.0	0.0%	0.8	4.9%	1.5	9.5%
Low Positive	80	33.3	1.4	4.1%	1.3	3.9%	1.5	4.5%	2.4	7.2%
Low Positive	80	34.0	1.3	3.8%	0.0	0.0%	1.5	4.4%	2.0	5.8%
Mid Positive	80	101.9	3.6	3.5%	2.1	2.1%	4.4	4.3%	6.1	5.9%
Mid Positive	80	133.3	4.9	3.6%	0.3	0.2%	6.4	4.8%	8.1	6.1%
High Positive	80	172.3	6.3	3.7%	0.0	0.0%	5.8	3.4%	8.5	5.0%
High Positive	80	207.9	11.0	5.3%	0.0	0.0%	16.0	7.7%	19.5	9.4%
Negative Control	80	1.9	0.08	4.5%	0.1	3.3%	0.1	6.1%	0.2	8.3%
Positive Control	80	55.6	1.5	2.8%	0.9	1.7%	2.1	3.8%	2.8	5.0%

BioPlex® 2200 Celiac IgG – Anti-DGP

Sample Type	N	Mean U/mL	Within Run		Between Run		Between Day		Total Precision	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
High Negative	80	10.1	0.4	4.0%	0.2	2.2%	0.4	3.9%	0.6	6.0%
High Negative	80	11.6	0.6	5.0%	0.6	4.8%	0.8	6.8%	1.1	9.7%
Near Cutoff	80	15.0	0.4	2.4%	0.3	2.3%	0.6	3.9%	0.8	5.1%
Near Cutoff	80	16.6	0.8	4.9%	0.5	3.1%	0.9	5.3%	1.3	7.8%
Low Positive	80	32.7	1.7	5.3%	0.0	0.0%	2.3	7.0%	2.9	8.8%
Low Positive	80	33.2	1.1	3.3%	0.0	0.0%	0.9	2.6%	1.4	4.2%
Mid Positive	80	89.7	4.1	4.6%	2.6	2.9%	6.1	6.8%	7.8	8.7%
Mid Positive	80	93.9	4.1	4.4%	0.0	0.0%	4.5	4.8%	6.1	6.5%
High Positive	80	164.6	4.8	2.9%	3.0	1.8%	4.8	2.9%	7.4	4.5%
High Positive	80	194.6	9.4	4.8%	2.9	1.5%	10.6	5.5%	14.5	7.4%
Negative Control	80	2.8	0.3	10.2%	0.0	0.0%	0.1	4.5%	0.3	11.2%
Positive Control	80	57.6	1.6	2.7%	1.4	2.4%	2.2	3.9%	3.0	5.3%

CLSI EP15-A2 Reproducibility

Precision and reproducibility was also evaluated in accordance with CLSI EP15-A2 guideline "User Verification of Performance for Precision and Trueness, Vol 25, No 17".

A different serum panel consisting of samples spanning the measuring range were assayed in 4 replicates per run, one run per day over 5 days (n=20). One positive and one negative control were included. The data were analyzed for within-run, between run (day), and total precision and the mean U/mL, standard deviation and percent coefficient of variation are summarized below:

BioPlex® 2200 Celiac IgA – Anti-tTG IgA

Panel Member	N	Grand Mean (U/mL)	Within Run		Between Run (Day)		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Negative	20	6.1	0.27	4.4%	0.00	0.0%	0.27	4.4%
Negative	20	6.3	0.26	4.1%	0.16	2.5%	0.30	4.8%
Near Cutoff	20	12.2	0.47	3.8%	0.29	2.3%	0.55	4.5%
Near Cutoff	20	15.7	0.67	4.3%	0.27	1.7%	0.72	4.6%
Low Positive	20	38.5	2.25	5.8%	0.75	2.0%	2.37	6.2%
Low Positive	20	40.1	3.02	7.5%	0.00	0.0%	3.02	7.5%

Panel Member	N	Grand Mean (U/mL)	Within Run		Between Run (Day)		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Medium Positive	20	84.9	3.86	4.6%	0.48	0.6%	3.89	4.6%
Medium Positive	20	111.9	4.39	3.9%	5.01	4.5%	6.66	6.0%
High Positive	20	207.9	9.67	4.6%	0.00	0.0%	9.67	4.6%
High Positive	20	219.1	7.88	3.6%	3.84	1.8%	8.77	4.0%
Negative Control	20	1.2	0.06	4.8%	0.00	0.0%	0.06	4.8%
Positive Control	20	67.4	4.02	6.0%	0.00	0.0%	4.02	6.0%

BioPlex® 2200 Celiac IgA – Anti-DGP IgA

Panel Member	N	Grand Mean (U/mL)	Within Run		Between Run (Day)		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Negative	20	4.3	0.15	3.6%	0.00	0.0%	0.15	3.6%
Negative	20	8.0	0.37	4.7%	0.00	0.0%	0.37	4.7%
Near Cutoff	20	15.4	0.39	2.5%	0.11	0.7%	0.41	2.6%
Near Cutoff	20	16.4	0.67	4.1%	0.00	0.0%	0.67	4.1%
Low Positive	20	32.4	1.25	3.8%	0.00	0.0%	1.25	3.8%
Low Positive	20	33.8	1.32	3.9%	0.00	0.0%	1.32	3.9%
Medium Positive	20	91.3	3.00	3.3%	0.95	1.0%	3.15	3.4%
Medium Positive	20	93.1	4.07	4.4%	2.70	2.9%	4.89	5.2%
High Positive	20	169.2	8.61	5.1%	0.00	0.0%	8.61	5.1%
High Positive	20	187.8	6.41	3.4%	0.00	0.0%	6.41	3.4%
Negative Control	20	2.0	0.11	5.6%	0.06	3.0%	0.13	6.3%
Positive Control	20	55.4	2.27	4.1%	0.52	0.9%	2.33	4.2%

BioPlex® 2200 Celiac IgG – Anti-tTG IgG

Panel Member	N	Grand Mean (U/mL)	Within Run		Between Run (Day)		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Negative	20	7.1	0.23	3.2%	0.16	2.3%	0.28	3.9%
Negative	20	7.2	0.27	3.8%	0.21	2.9%	0.34	4.8%
Near Cutoff	20	12.7	0.50	3.9%	0.24	1.9%	0.55	4.4%
Near Cutoff	20	14.8	0.66	4.5%	0.26	1.7%	0.71	4.8%
Low Positive	20	30.2	0.87	2.9%	0.47	1.5%	0.99	3.3%
Low Positive	20	31.4	0.85	2.7%	0.60	1.9%	1.04	3.3%
Medium Positive	20	94.2	2.93	3.1%	2.70	2.9%	3.99	4.2%
Medium Positive	20	123.2	5.72	4.6%	2.32	1.9%	6.18	5.0%
High Positive	20	164.1	8.81	5.4%	5.46	3.3%	10.36	6.3%
High Positive	20	189.7	8.58	4.5%	4.75	2.5%	9.81	5.2%
Negative Control	20	1.8	0.18	9.8%	0.00	0.0%	0.18	9.8%
Positive Control	20	51.5	1.44	2.8%	0.53	1.0%	1.53	3.0%

BioPlex® 2200 Celiac IgG – Anti-DGP IgG

Panel Member	N	Grand Mean (U/mL)	Within Run		Between Run (Day)		Total Precision	
			SD	%CV	SD	%CV	SD	%CV
Negative	20	9.7	0.25	2.5%	0.34	3.5%	0.42	4.3%
Negative	20	11.0	0.37	3.4%	0.00	0.0%	0.37	3.4%
Near Cutoff	20	14.3	0.52	3.6%	0.26	1.8%	0.58	4.0%
Near Cutoff	20	15.9	0.52	3.3%	0.29	1.8%	0.59	3.7%
Low Positive	20	30.6	1.01	3.3%	0.31	1.0%	1.06	3.5%
Low Positive	20	32.5	1.45	4.5%	0.71	2.2%	1.61	5.0%
Medium Positive	20	88.8	2.65	3.0%	0.64	0.7%	2.72	3.1%
Medium Positive	20	91.4	3.59	3.9%	3.36	3.7%	4.92	5.4%
High Positive	20	172.5	4.57	2.7%	2.45	1.4%	5.19	3.0%
High Positive	20	202.8	5.62	2.8%	4.86	2.4%	7.43	3.7%
Negative Control	20	2.7	0.23	8.6%	0.01	0.3%	0.23	8.6%
Positive Control	20	54.1	1.36	2.5%	0.65	1.2%	1.51	2.8%

Lot-to-lot Reproducibility

The lot-to-lot reproducibility study was conducted to evaluate the variation among the lots of the reagent kit. Serum samples spanning the assay range were tested with three reagent lots on three BioPlex 2200 instruments in replicates of 10 for two runs.

Each lot mean (U/mL) was calculated using data 60 points for each patient serum sample (ten replicates, three instruments, two runs per instrument). The lot to lot grand mean (U/mL), standard deviation and %CV of the anti-DGP and anti-tTG IgA samples were calculated for each of the samples.

BioPlex® 2200 Celiac IgA – Anti-tTG IgA

Sample ID	Mean U/mL	Within Run		Between Run		Between Instrument/ Operator		Between Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
SCePr14	7.2	0.35	4.8%	0.54	7.5%	0.00	0.0%	0.76	10.5%	1.00	13.8%
SCePr09	7.5	0.29	3.9%	0.52	6.9%	0.00	0.0%	0.87	11.6%	1.06	14.1%
SCePr02	14.6	0.54	3.7%	1.31	9.0%	0.00	0.0%	1.43	9.8%	2.01	13.8%
SCePr16	18.3	0.68	3.7%	1.64	9.0%	0.00	0.0%	1.32	7.2%	2.22	12.1%
SCePr19	39.5	2.28	5.8%	2.72	6.9%	0.73	1.9%	5.66	14.3%	6.72	17.0%
SCePr17	39.7	1.65	4.2%	2.65	6.7%	0.00	0.0%	2.56	6.4%	4.03	10.2%
SCePr08	86.0	3.97	4.6%	5.60	6.5%	0.00	0.0%	10.55	12.3%	12.58	14.6%
SCePr06	107.7	3.98	3.7%	9.35	8.7%	0.00	0.0%	11.35	10.5%	15.23	14.1%
SCePr07	196.6	9.12	4.6%	15.30	7.8%	0.00	0.0%	19.19	9.8%	26.18	13.3%
SCePr18	213.3	8.83	4.1%	18.58	8.7%	0.00	0.0%	13.43	6.3%	24.57	11.5%

BioPlex® 2200 Celiac IgA – Anti-DGP IgA

Sample ID	Mean U/mL	Within Run		Between Run		Between Instrument/ Operator		Between Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
SCePr09	1.5	0.10	6.3%	0.16	10.3%	0.00	0.0%	0.00	0.0%	0.19	12.1%
SCePr16	4.6	0.22	4.8%	0.42	9.2%	0.08	1.6%	0.05	1.0%	0.48	10.6%
SCePr14	15.4	0.67	4.3%	1.03	6.6%	0.00	0.0%	0.52	3.4%	1.33	8.6%
SCePr07	16.3	0.60	3.7%	0.76	4.6%	0.00	0.0%	0.44	2.7%	1.06	6.5%
SCePr03	33.3	1.22	3.7%	1.54	4.6%	0.00	0.0%	1.60	4.8%	2.54	7.6%
SCePr01	35.7	1.71	4.8%	2.00	5.6%	0.00	0.0%	1.78	5.0%	3.18	8.9%
SCePr22	99.3	4.38	4.4%	5.87	5.9%	0.00	0.0%	6.67	6.7%	9.90	10.0%
SCePr06	102.0	3.44	3.4%	5.05	4.9%	0.00	0.0%	9.16	9.0%	11.01	10.8%
SCePr05	188.9	6.86	3.6%	11.88	6.3%	0.00	0.0%	15.81	8.4%	20.93	11.1%
SCePr18	207.0	8.11	3.9%	13.87	6.7%	0.00	0.0%	12.66	6.1%	20.46	9.9%

BioPlex® 2200 Celiac IgG – Anti-tTG IgG

Sample ID	Mean U/mL	Within Run		Between Run		Between Instrument/ Operator		Between Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
SCePr14	3.9	0.25	6.5%	0.58	15.0%	0.00	0.0%	0.78	20.1%	1.00	25.9%
SCePr20	8.8	0.57	6.5%	1.11	12.5%	0.11	1.2%	0.00	0.0%	1.25	14.2%
SCePr16	15.9	0.85	5.4%	0.97	6.1%	0.00	0.0%	0.61	3.9%	1.43	9.0%
SCePr10	17.6	1.00	5.7%	2.33	13.3%	0.00	0.0%	0.00	0.0%	2.54	14.5%
SCePr01	34.2	1.71	5.0%	1.78	5.2%	0.83	2.4%	0.00	0.0%	2.60	7.6%
SCePr09	34.7	1.76	5.1%	1.89	5.4%	0.00	0.0%	3.11	9.0%	4.04	11.7%
SCePr13	76.2	4.09	5.4%	5.90	7.7%	0.00	0.0%	6.43	8.4%	9.64	12.6%
SCePr15	120.6	7.17	5.9%	8.99	7.5%	0.00	0.0%	14.11	11.7%	18.20	15.1%
SCePr06	178.2	11.02	6.2%	19.07	10.7%	0.00	0.0%	0.00	0.0%	22.02	12.4%
SCePr04	180.0	14.98	8.3%	10.88	6.0%	0.00	0.0%	27.05	15.0%	32.78	18.2%

BioPlex® 2200 Celiac IgG – Anti-DGP IgG

Sample ID	Mean U/mL	Within Run		Between Run		Between Instrument/ Operator		Between Lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
SCePr06	2.2	0.16	7.1%	0.37	16.8%	0.00	0.0%	0.00	0.0%	0.40	18.2%
SCePr07	10.2	0.59	5.7%	0.56	5.5%	0.20	2.0%	0.42	4.1%	0.94	9.2%
SCePr15	14.8	0.70	4.7%	0.72	4.9%	0.00	0.0%	0.36	2.4%	1.06	7.2%
SCePr10	15.5	0.83	5.3%	0.92	6.0%	0.00	0.0%	0.92	5.9%	1.54	9.9%
SCePr04	31.6	2.27	7.2%	1.87	5.9%	0.00	0.0%	0.00	0.0%	2.94	9.3%
SCePr14	32.6	1.45	4.5%	1.27	3.9%	0.99	3.0%	1.98	6.1%	1.27	3.9%
SCePr23	87.8	6.03	6.9%	7.48	8.5%	1.50	1.7%	0.92	1.0%	9.77	11.1%
SCePr13	92.1	4.82	5.2%	5.86	6.4%	0.00	0.0%	2.14	2.3%	7.88	8.6%
SCePr01	165.1	9.96	6.0%	8.50	5.1%	0.00	0.0%	18.97	11.5%	23.05	14.0%

SCePr20	197.7	15.26	7.7%	9.06	4.6%	0.00	0.0%	17.84	9.0%	25.16	12.7%

b. Linearity/assay reportable range:

Three low and high Celiac anti-tTG IgA or IgG and anti-DGP IgA or IgG positive patient serum samples were tested to demonstrate linearity. These samples were diluted with immunodepleted serum according to CLSI EP06-A. Each sample and dilution was evaluated in replicates of four using one Celiac IgA and IgG lot on one instrument. Linear and polynomial regression analysis of Celiac IgA and IgG recovery *vs.* sample dilution was performed to determine if the dilution curves exhibit statistically significant non-linear regression based on the CLSI guideline EP06-A.

The regression parameters (slope, intercept and r2) of the observed values vs. predicted values are show below.

Celiac Assays	Sample	Conc. (U/mL)	Slope	Intercept	r^2	Dilution range (U/mL)
Anti-tTG IgA	1	58.4	1.0001	-0.0016	0.9996	0.3 – 58.4
	2	68.7	1.0000	0.0011	0.9991	0.3 – 68.7
	3	61.8	1.0000	0.0005	0.9989	0.3 – 61.8
	4	263.0	1.0000	0.0016	0.9963	0.3 – 263.0
	5	235.1	1.0000	0.0016	0.9997	0.3 - 235.1
	6	254.1	1.0000	-0.0037	0.9984	0.3 – 254.1
Anti-DGP IgA	1	60.9	1.0000	0.0006	0.9992	0.0 – 60.9
	2	55.0	1.0001	-0.0016	0.9988	0.0 – 55.0
	3	72.6	1.0000	-0.0011	0.9969	0.0 – 72.6
	4	223.1	1.0000	0.0000	0.9997	0.0 - 223.1
	5	206.2	1.0000	0.0015	0.9987	0.0 – 206.2
	6	242.6	1.0000	0.0010	0.9995	0.0 - 242.6
Anti-tTG IgG	1	67.5	1.0000	0.0011	0.9999	0.5 – 67.5
	2	68.0	1.0000	-0.0006	0.9995	0.5 - 68.0
	3	46.7	1.0000	-0.0010	0.9977	0.5 – 46.7
	4	259.9	1.0000	-0.0050	0.9984	0.3 – 259.9
	5	232.7	1.0000	-0.0001	0.9987	0.3 – 232.7
	6	253.2	1.0000	-0.0017	0.9972	0.3 – 253.2
Anti-DGP IgG	1	48.5	1.0000	0.0016	0.9997	0.0 – 48.5
	2	57.9	1.0000	-0.0005	0.9989	0.0 – 57.9
	3	49.2	1.0000	0.0000	0.9982	0.0 – 49.2
	4	192.9	1.0000	-0.0017	0.9985	0.0 – 192.9
	5	183.4	1.0000	0.0000	0.9992	0.0 – 183.4
	6	238.6	1.0000	-0.0017	0.9984	0.0 – 238.6

BioPlex 2200 Celiac Assay	Assay Measuring Range
Anti-tTG IgA	0.5 to 250 U/mL
Anti-DGP IgA	0.2 to 250 U/mL
Anti-tTG IgG	0.8 to 250 U/mL
Anti-DGP IgG	0.4 to 250 U/mL

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability:
There is no international or certified reference material available for Celiac anti-tTG and anti-DGP IgA and IgG. The calibrators are assigned relative arbitrary units (U/mL).

Value Assignment:
The calibrators are manufactured independently from the controls, and are stabilized with ≤0.3% ProClin® 300, ≤0.1% sodium benzoate, and <0.1% sodium azide. Calibrator assignment is established for matched lots of BioPlex® 2200 Celiac IgA or IgG kit and calibrators using a master set of calibrators as reference and replicate analyses on multiple BioPlex® 2200 instruments. The BioPlex® 2200 Celiac IgA or IgG Reagent Kit is calibrated using a set of five (5) distinct calibrators for anti-tTG and anti-DGP IgG or IgA, which are used to establish points of reference for determining the presence of anti-tTG and anti-DGP IgA or IgG in human specimens.

The negative control is manufactured to give negative results with values below the cut-off for each assay. The positive control is manufactured to give positive results with values above the assay cut-off for each assay.

Stability:
Stability studies have been performed to support the following claims:

Calibrator and Control:
BioPlex® 2200 Celiac IgA and IgG Control and Calibrator Sets: Calibrator Open Vial Stability (2 to 8°C), 60 days from first opening; Control Open Vial Stability (2 to 8°C), 60 days from first opening; Calibration Curve On-board Stability, 30 days; Calibrators and Controls Real Time Stability (2 to 8°C), 9 months; labeled as until expiration date.

Kit Stability:
BioPlex® 2200 Celiac IgA and IgG Kit: Real Time (unopened) Kit Stability, 9 months or until the date of expiration when stored unopened on the instrument or at 2 to 8°C; The Open kit claim is 60 days.

Serum Sample Stability:
Sample stability studies were also performed: Sample stability fresh (2 to 8°C), 7 days; Sample stability frozen (-20 or -80°C), 8 months; Sample Freeze-thaw (-20 or -80°C), up to 3-freeze thaw cycles acceptable.

d. Detection limit:

The results of LoQ, LoD and LoB are summarized in the table below.

BioPlex® 2200 Celiac Assay	LoQ (U/mL)	LoD (U/mL)	LoB (U/mL)
Anti-tTG IgA	0.5	0.5	0.4
Anti-DGP IgA	0.2	0.1	0.0

BioPlex® 2200 Celiac Assay	LoQ (U/mL)	LoD (U/mL)	LoB (U/mL)
Anti-tTG IgG	0.8	0.8	0.6
Anti-DGP IgG	0.4	0.1	0.0

e. *Analytical specificity:*
An interfering substances study was conducted to evaluate the potential interference of specific endogenous and exogenous substances with the BioPlex® 2200 Celiac IgA and IgG kits according to CLSI EP7-A2.
No interference was observed with any of the substances tested, except anti-tTG IgA and IgG at hemolysate level above hemoglobin concentration of 63 mg/dL. The substances and the maximum levels tested are shown in the table below:

Substance	**Concentration**
Hemolysate	≤500 mg/dL*
Bilirubin (unconjugated)	≤20 mg/dL
Bilirubin (conjugated)	≤30 mg/dL
Triglycerides	≤3300 mg/dL
Total Protein	≤12 g/dL
Cholesterol	≤500 mg/dL
Red Blood Cells	≤0.4% (v/v)
Gamma-Globulin	≤6 g/dL
Beta-Carotene	≤0.6 mg/dL
Ascorbic Acid	≤3 mg/dL
EDTA	< 800 mg/dL

*for anti-DGP IgA and IgG only

Cross-Reactivity:
A cross-reactivity study was performed to determine if patient serum samples from individuals with various disease states and other potentially interfering factors interfere with test results from the BioPlex® 2200 Celiac IgA or IgG kit. Samples from individuals with known disease states for potential cross reactivity listed in the table below were evaluated with the BioPlex® 2200 Celiac IgA or IgG kit. The table below shows the number (N) of samples containing potential cross reactants as disease state evaluated by the BioPlex® Celiac IgA and IgG kits. The cross reactivity was obtained as the positivity rate from the ratio of the number of samples scored positive by the BioPlex® Celiac IgA and IgG assays to the total number of cross reactant samples evaluated.

Cross Reactive Disease State	N	BioPlex 2200							
		Anti-tTG IgA		Anti-DGP IgA		Anti-tTG IgG		Anti-DGP IgG	
		Pos (+)	% Positivity	Pos (+)	% Positivity	Pos (+)	% Positivity	Pos (+)	% Positivity
Chronic Active Hepatitis	20	0	0%	0	0%	5	25%	0	0%
Crohn's Disease	23	1	4%	1	4%	0	0%	0	0%
Diabetes Mellitus Type 1	20	0	0%	0	0%	0	0%	0	0%
Gastritis	20	0	0%	0	0%	0	0%	0	0%
Graves'/Hashimoto's Disease	23	0	0%	1	4%	0	0%	1	4%
Irritable Bowel Syndrome	15	0	0%	0	0%	0	0%	0	0%
Pernicious Anemia	6	0	0%	0	0%	0	0%	0	0%
Primary Biliary Cirrhosis	19	0	0%	0	0%	0	0%	2	11%
Rheumatoid Arthritis	20	1	5%	2	10%	1	5%	1	5%
Scleroderma	21	0	0%	1	5%	0	0%	1	5%
Sjögren's Syndrome	24	0	0%	1	4%	1	4%	1	4%
Syphilis	10	0	0%	1	10%	0	0%	0	0%
Systemic Lupus Erythematosus	30*	0	0%	0	0%	0	0%	0	0%
Ulcerative Colitis	22	0	0%	0	0%	0	0%	0	0%

* 1 sample exhibited repeated instrument error flags and was excluded from the anti-tTG IgA and IgG data analysis

f. Assay cut-off:

The assay cutoff values were determined by performing Receiver Operator Characteristic (ROC) analysis using clinically diagnosed serum samples. The study to determine the Celiac IgA or IgG assay cutoff was comprised of two patient serum sample groups –123 samples from patients diagnosed with celiac disease and 112 from non-celiac or other rheumatic disease control donors. The assay cut-off values were confirmed by testing 298 samples from apparently healthy donors.

A cutoff of 15.0 U/mL for anti-tTG IgA or IgG and for anti-DGP IgA or IgG was established by optimizing for clinical accuracy.

2. Comparison studies:

a. Method comparison with predicate device:
The performance of the BioPlex® 2200 Celiac IgA and IgG kits was evaluated including 156 patients diagnosed with celiac disease 163 patients with other

rheumatic or non-CD disease control, 11 celiac IgA deficient patients, and 16 dermatitis herpetiformis (DH) patients. Results from all patient serum samples of both the new and the predicate immunoassays are compared. Results are summarized in the tables below:

All Retrospective Patient Serum Samples

BioPlex 2200 Celiac IgA

		Predicate IgA EIA Kit		
		Positive	Negative	Total
anti-tTG IgA	Positive	163	0	163
	Negative	6	176	182
	Total	169	176	345*
anti-DGP IgA	Positive	144	13	157
	Negative	4	185	189
	Total	148	198	346

* 1 sample exhibited repeated instrument error flags and was excluded from the data analysis

Anti-tTG IgA Positive Agreement (95% CI) = 96.4% (163/169) (92.5 – 98.4%)
Anti-tTG IgA Negative Agreement (95% CI) = 100% (176/176) (97.9 - 100%)
Anti-tTG IgA Total Agreement (95% CI) = 98.3% (339/345) (96.3 – 99.2%)
Anti-DGP IgA Positive Agreement (95% CI) = 97.3% (144/148) (93.3 – 98.9%)
Anti-DGP IgA Negative Agreement (95% CI) = 93.4% (185/198) (89.1 – 96.1%)
Anti-DGP IgA Total Agreement (95% CI) = 95.1% (329/346) (92.3 – 96.9%)

BioPlex 2200 Celiac IgG

		Predicate IgG EIA Kit		
		Positive	Negative	Total
anti-tTG IgG	Positive	56	36	92
	Negative	4	249	253
	Total	60	285	345*
anti-DGP IgG	Positive	140	17	157
	Negative	10	179	189
	Total	150	196	346

* 1 sample exhibited repeated instrument error flags and was excluded from the data analysis

Anti-tTG IgG Positive Agreement (95% CI) = 93.3% (56/60) (84.1– 97.4%)
Anti-tTG IgG Negative Agreement (95% CI) = 87.4% (249/285) (83.0 – 90.7%)
Anti-tTG IgG Total Agreement (95% CI) = 88.4% (305/345) (84.6 – 91.4%)
Anti-DGP IgG Positive Agreement (95% CI) = 93.3% (140/150) (88.2 – 96.3%)

Anti-DGP IgG Negative Agreement (95% CI) = 91.3% (179/196) (86.6 – 94.5%)
Anti-DGP IgG Total Agreement (95% CI) = 92.2% (319/346) (88.9 – 94.6%)

Results from values in the measuring range and 10% of diluted total samples of both the new and the predicate immunoassays are compared. Results are summarized in the tables below:

Results within the measuring range and 10% of diluted serum samples

BioPlex 2200 Celiac IgA

		Predicate IgA EIA Kit		
		Positive	Negative	Total
anti-tTG IgA (0.5 – 250 U/mL)	Positive	97	0	97
	Negative	6	108	114
	Total	103	108	211
anti-DGP IgA (0.2 – 250 U/mL)	Positive	129	13	142
	Negative	4	164	168
	Total	133	177	310

Anti-tTG IgA Positive Agreement (95% CI) = 94.2% (97/103) (87.9 – 97.3%)
Anti-tTG IgA Negative Agreement (95% CI) = 100% (108/108) (96.6 - 100%)
Anti-tTG IgA Total Agreement (95% CI) = 97.2% (205/211) (93.9 – 98.7%)
Anti-DGP IgA Positive Agreement (95% CI) = 97.0% (129/133) (92.5 – 98.8%)
Anti-DGP IgA Negative Agreement (95% CI) = 92.7% (164/177) (87.8 – 95.7%)
Anti-DGP IgA Total Agreement (95% CI) = 94.5% (293/310) (91.4 – 96.5%)

BioPlex 2200 Celiac IgG

		Predicate IgG EIA Kit		
		Positive	Negative	Total
anti-tTG IgG (0.8 – 250 U/mL)	Positive	54	36	90
	Negative	4	194	198
	Total	58	230	288
anti-DGP IgG (0.4 – 250 U/mL)	Positive	140	17	157
	Negative	9	82	91
	Total	149	99	248

Anti-tTG IgG Positive Agreement (95% CI) = 93.1% (54/58) (83.6 – 97.3%)
Anti-tTG IgG Negative Agreement (95% CI) = 84.3% (194/230) (79.1 – 88.5%)
Anti-tTG IgG Total Agreement (95% CI) = 86.1% (248/288) (81.6 – 89.6%)
Anti-DGP IgG Positive Agreement (95% CI) = 94.0% (140/149) (88.9 – 96.8%)
Anti-DGP IgG Negative Agreement (95% CI) = 82.8% (82/99) (74.2 – 89.0%)
Anti-DGP IgG Total Agreement (95% CI) = 89.5% (222/248) (85.1 – 92.7%)

b. Matrix comparison:

Not Applicable- Serum only.

3. Clinical studies:

a. Clinical Sensitivity and specificity:

The clinical studies involved testing 319 serum specimens including 163 non-Celiac disease control patients and 156 diagnosed Celiac disease patients. The BioPlex® 2200 Celiac IgA and IgG sensitivity and specificity are shown below:

BioPlex 2200 Celiac IgA

		Clinical Diagnosis		
		Positive	Negative	Total
anti-tTG IgA	Positive	148	2	150
	Negative	8	160	168
	Total	156	162	318*
anti-DGP IgA	Positive	136	5	141
	Negative	20	158	178
	Total	156	163	319

* 1 sample exhibited repeated instrument error flags and was excluded from the data analysis

Anti-tTG IgA Sensitivity (95% CI) = 94.9% (148/156) (90.2 – 97.4%)
Anti-tTG IgA Specificity (95% CI) = 98.8% (160/162) (95.6 – 99.7%)
Anti-DGP IgA Sensitivity (95% CI) = 87.2% (136/156) (81.0 – 91.5%)
Anti-DGP IgA Specificity (95% CI) = 96.9% (158/163) (93.0 – 98.7%)

BioPlex 2200 Celiac IgG

		Clinical Diagnosis		
		Positive	Negative	Total
anti-tTG IgG	Positive	69	7	76
	Negative	87	155	242
	Total	156	162	318*
anti-DGP IgG	Positive	132	5	137
	Negative	24	158	182
	Total	156	163	319

* 1 sample exhibited repeated instrument error flags and was excluded from the data analysis

Anti-tTG IgG Sensitivity (95% CI) = 44.2% (69/156) (36.7 – 52.1%)

Anti-tTG IgG Specificity (95% CI) = 95.7% (155/162) (91.4 – 97.9%)
Anti-DGP IgG Sensitivity (95% CI) = 84.6% (132/156) (78.1 – 89.4%)
Anti-DGP IgG Specificity (95% CI) = 96.9% (158/163) (93.0 – 98.7%)

Serum samples from patients previously diagnosed with celiac disease and IgA deficiency (N=11) were run on the BioPlex 2200 Celiac IgG kits and the # positive samples is shown in the table below:

Patient Group	**# Positive Anti-tTG IgG (%)**	**# Positive Anti-DGP IgG (%)**
Celiac Disease with IgA deficiency	9 (81.8%) 95% CI: 52.3 – 94.9%	8 (72.7%) 95% CI: 43.4 – 90.3%

The positive rates of the BioPlex Celiac IgA and IgG in each of disease category are shown below.

Disease Category	Number Enrolled	Anti-tTG IgA	Anti-DGP IgA	Anti-tTG IgG	Anti-DGP IgG
Celiac Disease	156	148 (94.9%)	136 (87.2%)	69 (44.2%)	132 (84.6%)
Apparently Healthy Subject	300	0 (0.0%)	5 (1.7%)	2 (0.7%)	5 (1.7%)
IgA Deficiency	11	0 (0.0%)	0 (0.0%)	9 (81.8%)	8 (72.7%)
Dermatitis Herpetiformis	16	13 (81.3%)	16 (100%)	7 (43.8%)	12 (75.0%)
Chronic Active Hepatitis	10	0 (0%)	0 (0%)	5 (50%)	0 (0%)
Crohn's Disease	13	1 (7.7%)	0 (0%)	0 (0%)	0 (0%)
Diabetes Mellitus Type 1	10	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gastritis	10	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Graves'/Hashimoto's Disease	13	0 (0%)	1 (7.7%)	0 (0%)	0 (0%)
Irritable Bowel Syndrome	15	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pernicious Anemia	6	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Primary Biliary Cirrhosis	9	0 (0%)	0 (0%)	0 (0%)	2 (22.2%)
Rheumatoid Arthritis	10	1 (10%)	1 (10%)	1 (10%)	1 (10%)
Scleroderma	11	0 (0%)	1 (9.1%)	0 (0%)	1 (9.1%)
Sjögren's Syndrome	14	0 (0%)	1 (7.1%)	1 (7.1%)	1 (7.1%)
Systemic Lupus Erythematosus	20*	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ulcerative Colitis	12	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Disease Category	Number Enrolled	Anti-tTG IgA	Anti-DGP IgA	Anti-tTG IgG	Anti-DGP IgG
Syphilis	10	0 (0%)	1 (10%)	0 (0%)	0 (0%)

* 1 sample exhibited repeated instrument error flags and was excluded from the anti-tTG IgG and IgA data analysis

c. Other clinical supportive data (when a. and b. are not applicable):

Refer to Method Comparison

4. Clinical cut-off:
See Assay Cutoff

5. Expected values/Reference range:
Three hundred serum samples from apparently healthy donors including 139 males ranging in age from <1 to 94 and 161 females ranging in age from 5 to 101 were tested with BioPlex® 2200 Celiac IgA and IgG kits. The number of positive and mean value of the BioPlex® Celiac IgA and IgG results are shown below.

Assay	N (%Positive)	Mean (U/mL)
anti-tTG IgA	0 (0.0%)	0.6
anti-DGP IgA	5 (1.7%)	2.2
anti-tTG IgG	2 (0.7%)	2.3
anti-DGP IgG	5 (1.7%)	1.7

Results of <15.0 U/mL for anti-tTG IgA or IgG and for anti-DGP IgA or IgG are reported as negative and results ≥15.0 U/mL for anti-tTG IgA or IgG and for anti-DGP IgA or IgG are reported as positive.

Each laboratory should establish its own reference range pertinent to their specific patient populations.

Instrument Name:
The BioPlex 2200 System, software version 4.1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

BIO-RAD LABORATORIES, INC.
C/O DR. JUANG WANG
REGULATORY AFFAIRS REPRESENTATIVE
5500 EAST 2ND ST.
BENICIA, CA 94510

September 19, 2013

Re: K130053
Trade/Device Name: BioPlex® 2200 Celiac IgA kit
BioPlex® 2200 Celiac IgG kit
BioPlex® 2200 Celiac IgA Calibrator Set
BioPlex® 2200 Celiac IgG Calibrator Set
BioPlex® 2200 Celiac IgA Control Set
BioPlex® 2200 Celiac IgG Control Set
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: II
Product Code: MVM, MST, JIX, JJX
Dated: August 22, 2013
Received: August 23, 2013

Dear Dr. Wang:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Maria M. Chan -S

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgA Kit

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgA kit is an in vitro multiplex flow immunoassay intended for the semi-quantitative detection of IgA autoantibodies to deamidated gliadin peptide (DGP) and tissue Transglutaminase (tTG) in human serum. In conjunction with clinical findings and other diagnostic tests, the test system is used as an aid in the diagnosis of Celiac Disease (gluten-sensitive enteropathy).

The BioPlex 2200 Celiac IgA kit is intended for use with the Bio-Rad BioPlex 2200 System.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Maria M. Chan -S

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgA Control Set

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgA Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and the BioPlex 2200 Celiac IgA Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Celiac IgA Control Set has not been established with any other anti-tissue Transglutaminase (tTG) and anti-deamidated gliadin peptide IgA assays.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

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Expiration Date: December 31, 2013
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510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgA Calibrator Set

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgA Calibrator Set is intended for the calibration of the BioPlex 2200 Celiac IgA Reagent Pack.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

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Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgG Control Set

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgG Control Set is intended for use as an assayed quality control to monitor the overall performance of the BioPlex 2200 Instrument and the BioPlex 2200 Celiac IgG Reagent Pack in the clinical laboratory. The performance of the BioPlex 2200 Celiac IgG Control Set has not been established with any other anti-tissue Transglutaminase (tTG) and anti-deamidated gliadin peptide IgG assays.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

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Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgG Calibrator Set

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgG Calibrator Set is intended for the calibration of the BioPlex 2200 Celiac IgG Reagent Pack.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

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Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
K130053

Device Name
BioPlex® 2200 Celiac IgG Kit

Indications for Use *(Describe)*
The BioPlex 2200 Celiac IgG kit is an in vitro multiplex flow immunoassay intended for the semi-quantitative detection of IgG autoantibodies to deamidated gliadin peptide (DGP) and tissue Transglutaminase (tTG) in human serum. In conjunction with clinical findings and other diagnostic tests, the test system is used as an aid in the diagnosis of Celiac Disease (gluten-sensitive enteropathy).

The BioPlex 2200 Celiac IgG kit is intended for use with the Bio-Rad BioPlex 2200 System.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 807 Subpart C)

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